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3-20-03

This application is a divisional of pending US patent application serial number 09/592,595 filed June 12, 2000, which is a continuation-in-part of US patent application serial number 09/258,928 filed March 1, 1999 (now US patent number 6,218,120), which is a continuation in part of US patent application serial number 08/738,000 filed February 12, 1997 (now US patent number 6,074,821), <sup>which is the national stage of International Application</sup> ~~which claims priority from PCT/CA 95/00314, filed May 25, 1995, and GB 9410620.0, filed May 26, 1994.~~ <sup>which claims priority to</sup>

Please replace the paragraph on page 60, line 8, through page 61, line 9, of the specification with the following paragraph that has been re-written in clean form.

P2

Patients with spina bifida and mothers of patients were recruited from the Spina Bifida Clinic at the Montreal Children's Hospital following approval from the Institutional Review Board. Control children and mothers of controls were recruited from the same institution. Blood samples were used to prepare DNA from peripheral leukocytes, to assay MTHFR activity in lymphocyte extracts, and to measure total plasma homocysteine (tHcy). The presence of the C677T mutation (A to V) was evaluated by PCR and HinfI digestion (2). The A1298C mutation was initially examined by PCR and MboII digestion (5). The silent mutation, T1317C, was identified by SSCP and sequence analysis in a patient with severe MTHFR deficiency and homocystinuria. This patient, an African-American female, already carries a previously-described splice mutation (patient 354 (8)). Since this mutation also creates a MboII site and results in a digestion pattern identical to that of the A1298C mutation, distinct artificially-created restriction sites were used to distinguish between these 2 mutations. Detection of the A1298C polymorphism was performed with the use of the sense primer 5'-GGGAGGAGCTGACCAAGTGCAG-3' (SEQ ID NO:15) and the antisense primer (5'-GGGGTCAGGCCAGGGGCAG-3', SEQ ID NO:16), such that the 138bp PCR fragment was digested into 119bp and 19bp fragments by Fnu4HI in the presence of the C allele. An antisense primer (5'-GGTTCTCCCGAGAGGTAAAGATC-3', SEQ ID NO:17), which introduces a TaqI site, was similarly designed to identify the C allele of the T1317C polymorphism. Together with a sense primer (5'-CTGGGGATGTGGTGGCACTGC-3', SEQ ID NO:18), the 227bp fragment is digested into 202bp and 25bp fragments.

Kindly insert the enclosed sequence listing at the end of the application.